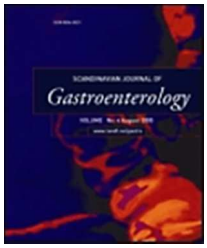

Phase angle as a prognostic marker after percutaneous endoscopic gastrostomy (PEG) in a prospective cohort study

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Complete List of Authors:	Martin, Lena; Karolinska Institutet, Department of Molecular medicine and Surgery; Karolinska Institutet, Department of Biosciences and Nutrition; Karolinska Universitetssjukhuset, Department of Clinical Nutrition and Dietetics Lagergren, Jesper; Karolinska Institutet, Department of Molecular medicine and Surgery, ; King\'s College London Division of Cancer Studies Blomberg, John; Karolinska Institutet, Department of Clinical Science, Intervention and Technology (CLINTEC), ; Karolinska University Hospital, , Center for Digestive Diseases johar, asif; Karolinska Institutet, Department of Molecular medicine and Surgery, Bosaeus, Ingvar; Sahlgrenska University Hospital, Department Clinical Nutrition ; University of Gothenburg, Sahlgrenska Academy Lagergren, Pernilla; Karolinska Institutet, Department of Molecular medicine and Surgery; King\'s College London Division of Cancer Studies
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Phase angle as a prognostic marker after percutaneous endoscopic gastrostomy (PEG) in a prospective cohort study

Short title: Phase Angle at time for PEG

Authors: Lena Martin[1,2,3], RD, PhD., Jesper Lagergren[4,5], MD, PhD., John Blomberg[6,7], MD, PhD., Asif Johar[1], Ingvar Bosaeus[8], MD, PhD., Pernilla Lagergren[1,5], RN, PhD.

1. Surgical Care Science, Department of Molecular medicine and Surgery, Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden.

2. Department of Biosciences and Nutrition, Karolinska Institutet, Karolinska University Hospital, 141 83 Huddinge, Sweden

3. Department of Clinical Nutrition and Dietetics, Karolinska University Hospital, 141 86 Stockholm, Sweden.

4. Upper Gastrointestinal Surgery, Department of Molecular medicine and Surgery, Karolinska Institutet, SE-171 76 Stockholm, Sweden.

5. Division of Cancer Studies, King's College London, London, United Kingdom.

6. Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Karolinska University Hospital, 141 83 Huddinge, Sweden

7. Center for Digestive Diseases, Karolinska University Hospital, SE-141 86 Stockholm, Sweden.

8. Department Clinical Nutrition at Sahlgrenska University Hospital, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden

Corresponding author:

Lena Martin, Registered dietician and PhD

Surgical Care Science, Department of Molecular medicine and Surgery,

Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden

e-mail address: lena.martin@ki.se

Abstract

***Objective*:** The phase angle identifies changes in tissue's electrical properties assessed by bioelectrical impedance measurement and it can predict prognosis in some conditions. Percutaneous endoscopic gastrostomy (PEG) is commonly used in patients with severe nutritional problems, but there is a need to improve the clinical decision-making for using PEG. We examined if a decreased phase angle predicts complications, short-term mortality (within 60 days of PEG insertion), or inflammatory markers (high C-reactive protein [CRP] levels or low albumin levels) following PEG insertion.

Material and Methods: The phase angle was assessed from body resistance and reactance as measured by bioelectrical impedance in 131 patients admitted for PEG. Anthropometrics and clinical biochemical measures were collected at the time of PEG insertion, while complications and mortality were assessed at clinical follow-ups. Multivariable logistic regression analysis provided odds ratios (ORs) with 95% confidence intervals (CIs) adjusted for sex, age, body mass index and comorbidity.

Results: A decreased phase angle did not statistically significantly increase the probability of acute complications or short-term mortality, but predicted increased inflammatory markers (CRP ≥10 mg/L (OR 1.63, 95% CI 1.02-2.60), albumin <30g/L (OR 2.10, 95% CI 1.24-3.57) and a combination of CRP ≥10 mg/L and albumin <30g/L (OR 3.06, 95% CI 1.51-6.19)).

Conclusions: A decreased phase angle did not predict acute complications or short-term mortality after PEG insertion, but predicted increased levels of inflammatory markers.

Keywords: complications; early mortality; enteral nutrition; malnutrition.

Introduction

Percutaneous endoscopic gastrostomy (PEG) is a procedure undertaken for those in need of nutritional supplementation over a longer or lifelong perspective, e.g. patients with cancer or neurological diseases (1, 2). The insertion of a PEG is usually technically easy, yet the procedure entails a complication rate of about 50% (3). A wide range of complications may occur, including leakage from the stoma in the abdominal wall and deeper situated infections with high risk of mortality. A combination of high C-reactive protein (CRP) and low albumin levels at the time of PEG insertion are markers of more vulnerable patients at a substantial risk of mortality (4). Old age, low body mass index (BMI) and comorbidity are other risk factors for severe complications after PEG insertion (5-7). Moreover in some situations decisions about inserting a PEG must include serious ethical considerations, e.g., in patients with dementia or in patients who are expected to die within a limited time frame (8, 9)

The phase angle is measured by bioelectrical impedance, which estimates the body composition (10) by measurement of body resistance and reactance to electrical current. While resistance depends on the bodily fluid and electrolyte content, the reactance is produced by cell membranes when storing parts of charge as a capacitor. The phase angle measures the cell membrane function obtained from the relation between resistance and reactance at 50 kHz. The phase angle is a direct and objective parameter without need for data on weight and height (11), which can predict prognosis in a variety of diseases.

The aim of the present study was to determine if phase angle predicts acute complications, short-term mortality and increased levels of inflammatory markers (high CRP levels and/or low albumin levels) after insertion of PEG, which could guide the clinical decision-making.

Methods

Study design

This was a prospective cohort study carried out at the Karolinska University Hospital in Stockholm, Sweden. The exposure was phase angle and the outcomes were acute complications, short-term mortality, high CRP levels and low albumin levels. The data collection has been described in detail elsewhere (12). In brief, consecutive patients requiring PEG were prospectively included in the study before PEG insertion. Patients were excluded if they declined, if for any reason it was not possible to perform the bioelectrical impedance spectroscopy measurement, or if the patients had a contraindication for bioelectrical impedance measurement (metal prostheses or cardiac failure). For each patient, clinical and treatment-related data were collected prior to PEG insertion according to a predefined study protocol to ensure completeness and uniformity, and blood samples were drawn before the PEG insertion for analyses of CRP and albumin. Weight was measured using a sitting weighing scale and height by half demi span (measured from the fingertip to the sternal notch using the left arm whenever possible) (13); BMI (kg/m2) was then calculated. All patients routinely fasted for 6 hours before the PEG procedure. The patients were followed up at a specialised clinic after PEG insertion.

Exposure – phase angle

The study exposure was the phase angle value just before the insertion of the PEG. Bioelectrical impedance spectroscopy (BodyScout, Fresenius Kabi) was used to assess the phase angle at 50 kHz. Just before the PEG insertion, the bioelectrical impedance measurement was carried out by a trained nurse or dietitian. The participants were resting in the supine position for at least 5 minutes before the tetrapolar whole body measurement, with electrodes on the dorsal surface of the hand/wrist and the foot/ankle of the same side

according to the manufacturer's instructions. Four electrodes for single use were used. Phase angle was calculated directly from the reactance and resistance. Phase angle is between 5° and 7° in healthy subjects (14). The higher the reactance, the higher the phase angle for any given resistance.

Outcomes

The primary outcomes were acute complications (yes/no) within 14 days of PEG insertion and mortality (yes/no) occurring within 60 days of PEG insertion. Acute complications were defined as peristomal infections, leakage, obstipation and abdominal pain and assessed at follow-up visits at 7 and 14 days post-PEG. Mortality within 60 days was assessed by linkages of personal identity numbers through the Swedish Registry of the Total Population. Secondary outcomes were increased CRP (≥ 10 mg/L), decreased albumin (<30 g/L) or a combination of the two.

Statistical analysis

Multivariable logistic regression analyses were used to estimate odds ratios (ORs) with 95% confidence intervals (CIs). Phase angle was expressed as a linear dependent variable in this model. Adjustments were made for sex (male or female), age (<65 or ≥65 years), BMI (<20 or ≥20) and comorbidity (cancer or other comorbidity [cardiovascular disease, neurological disease, or diabetes]). All statistical analyses were performed using the statistical software SAS (Statistical Package 9.3; SAS Institute Inc, Cary, NC).

Ethics

Patients, often together with a caregiver or attending relatives, gave informed consent to

participate in the study. The study was approved by the Regional Ethical Review Board in Stockholm, Sweden.

Results

Patients

Among 270 patients receiving a PEG during the study period, 131 (49%) were included in the present study. Non-participation (n=139) was due to technical problems, patients declining participation, or the presence of metal prostheses or cardiac failure. Characteristics of the participants are presented in Table 1. Most patients were male and younger than 65 years and had cancer as the indication for PEG. One third of patients were underweight (BMI <20) at the time of PEG insertion. The median phase angle was 4.8, and was slightly lower in women (4.3) than men (4.8) (Table 1).

Decreased phase angle in relation to outcomes

The results from the multivariable model are presented in Table 2. There were no statistically significant associations between decreased phase angle and risk of complications (OR 0.91, 95% CI 0.59-1.38) or mortality (OR 0.93, 95% CI 0.37-2.37). Decreased phase angle was moderately to strongly associated with increased CRP and decreased albumin levels. A one unit decrease in phase angle was associated with an increased risk of elevated CRP levels (OR 1.63, 95% CI 1.02 -2.60) and low albumin levels (OR 2.10, 95% CI 1.24-3.57), as well as a substantially increased risk of having a combination of increased CRP and decreased albumin (OR 3.06, 95% CI 1.51-6.19).

Discussion

This study indicates that a decreased phase angle at the time for PEG insertion is associated with markers of inflammation - an increase in CRP, decreased albumin as well as both of these outcomes combined, but it did not predict the occurrence of acute complications or mortality within 60 days of PEG insertion.

Strengths of the study include the prospective design, the valid data on the exposure and all outcomes, including objectively measured levels of CRP and albumin. Moreover, changes in phase angle might depend on sex, age, BMI and comorbidity and it was therefore an advantage that these variables were adjusted for in the multivariable model. Weaknesses include potential non-random non-participation, which introduces a risk of selection bias from including more healthy patients. Even though the cohort of 131 subjects is large when comparing with similar studies regarding bioelectrical impedance measurements, the statistical power to assess the outcomes complications and mortality was limited. Thus, the negative findings should be interpreted with caution. Another limitation is that different cut-off values have been used in the literature to assess for phase angle in relation to diagnosis-specific study populations (15). These might not be applicable for populations in a more general clinical situation (16) like for the heterogenic PEG population. To avoid this problem we instead used phase angle as a linear variable. Moreover, it should be acknowledged that complications might not only be due to the PEG insertion *per se*, but also be caused by metabolic disturbances related to refeeding of malnourished patients (17).

Our results showed that a decreased phase angle was associated with a high CRP, a universally accepted indicator of systemic inflammation. Phase angle may be directly affected by a change in electric tissue properties due to the disease itself, inflammation or malnutrition, among others. The strong association between a decrease in phase angle and low albumin

levels in the present study might also be due to inflammation, rather than an indicator for malnutrition (18, 19), as it has historically been described (20). These associations are of clinical relevance since CRP and albumin levels have been shown to predict mortality following PEG insertion (5). This finding together with the simplicity and objectivity in the assessment of the phase angle indicate a potential role in the clinical decision-making in patients considered for PEG.

In conclusion, a decreased phase angle reflects increased levels of inflammatory markers - CRP, albumin and a combination of the two. These biomarkers indicate worse outcomes following PEG. However, if the measurement of the phase angle actually facilitates clinical decision-making for PEG remains uncertain.

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Conflict of interest: None declared.

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Table 1. Characteristics of 131 study patients receiving a percutaneous endoscopic gastrostomy (PEG)

	Number	Per cent
Sex		
Female	46	35
Male	85	65
Age		
<65	75	5
>=65	56	43
Body mass index		
<20	41	31
>=20	90	69
Diagnosis		
Cancer	109	83
No cancer	22	17
Other diagnosis	30	23
No other diagnosis	101	77
Complications within 14 days of PEG		
No	89	68
Yes	42	32
Mortality within 60 days of PEG		
No	124	95
Yes	7	5
CRP level (mg/L)		
<10	78	60
>=10	47	36
missing	6	5
Albumin level (g/L)		
>30	92	70
<30	32	24
missing	7	5
C-reactive protein level >=10 and albumin>=30		
No	99	76
Yes	25	19

missing	7	5
Phase angle median		
Grouped	4.8	
Female	4.3	
Male	4.8	

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Table 2. Phase angle in relation to outcome variables in study patients receiving a percutaneous endoscopic gastrostomy (PEG)

	Patients Number	Odds ratio*	95% confidence interval
Acute complications			
No	89	1	Reference
Yes	42	0.91	0.59 – 1.38
Mortality within 60 days of PEG			
No	124	1	Reference
Yes	7	0.93	0.37 – 2.37
CRP			
< 10	78	1	Reference
≥10	47	1.63	1.02 – 2.60
Albumin			
≥30	92	1	Reference
< 30	32	2.10	1.24 – 3.57
CRP and albumin			
CRP<10 and albumin ≥ 30	70	1	Reference
CRP≥10 and albumin < 30	25	3.06	1.51 – 6.19

* Adjusted for sex, age, body mass index and comorbidity.